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EXAMINER
EPPERSON, JON D

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/578,282	Applicant(s) BEECHER ET AL.	
File Copy	Examiner Jon D Epperson	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,12,14,15,52-54,56-60,70,71 and 73-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,12,14,15,52-54,56-60,70,71 and 73-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Claims 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are currently pending. Applicants amended claims 1, 52, 59, 70 and 75 in Paper No. 21. Therefore, claims 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are pending and active in the instant application. An action on the merit follows.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Withdrawn Objections/Rejections

2. With respect to the rejections under the second paragraph of 35 U.S.C. 112, the rejections denoted Q, R (formerly A in the "New Rejections" of Paper No. 19, renamed so as to avoid confusion with the original A), S (formerly B in the "New Rejections "of Paper No. 19, renamed so as to avoid confusion with the original B) are withdrawn in view of applicant's amendments to the claims and/or cancellation of claims. The New Matter rejection under 35 U.S.C. 112, first paragraph is hereby withdrawn in view of Applicants' amendments and/or arguments. The Written Description rejection under 35 U.S.C. 112, first paragraph is hereby withdrawn in view of Applicants' amendments and/or arguments (Please note that a new "Written Description"

rejection is provided addressing a separate issue, see below). All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

35 USC 112, second paragraph

3. Claims 1-3, 6, 12, 14-15, 52-60 and 70-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A-O. Withdrawn.
P. The term "masked acid" in claims 3 and 54 is not defined by the claim or the specification and is indefinite and/or unclear. What set of acids does the term "masked" include? For example, in one preferred embodiment, Applicants state that a masked acid include [but are not limited to] compounds that function as "autocatalysts" (see specification, page 20, line 280 - page 21, line 1). Here, the Examiner contends that the "masked acids" in these claims are not defined with any chemical or physical characteristic, but only by functional properties i.e., their ability to "function" as an autocatalyst. A claim to a material defined solely in terms of what it can do, or a property thereof, does not particularly point out the claimed invention. A person of skill in the art cannot immediately envision all the possible chemical structures for "masked acid" with this an "autocatalytic" function. Thus, the metes and bounds of the claimed invention cannot be determined. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169. Therefore, claim 3, 54 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.
Q. Withdrawn.
R (formerly A in Paper No. 19). Withdrawn.
S (formerly B in Paper No. 19). Withdrawn.

Response to Arguments

4. Applicant's arguments have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

For ***claims 3 and 54*** (***paragraph P***), applicants reiterate their arguments by pointing to various places in the specification that provide examples of "masked" acids i.e., page 20, line 28-

page 21, line 1 wherein they also disclose a preferred embodiment i.e., 1,4-cyclohex-2-3-enediylbis(pentafluorobenzoate) (see Paper No. 21, page 8-9). Applicants further make an attempt to define what a "masked" acid is by stating, "masked acids comprise all acids, esters, anhydrides or nitrites capable of removing an acid-labile protecting group" (see Paper No. 21, page 9, paragraph 1).

It is the examiner's position that the specification or claims do not "define" what a masked acid is i.e., Applicants definition above is NOT in the specification (i.e., "masked acids comprise all acids ... capable of removing an acid-labile protecting group", see rejection above) and even if it were it would NOT be sufficient to adequately describe the claimed invention. Here, Applicants are defining the acid in terms of its "functional" properties i.e., what it can do (remove an acid-labile protecting group) and are NOT providing any distinguishing "structural" features that would characterize these acids. A claim to a material defined solely in terms of what it can do, or a property thereof, does not particularly point out the claimed invention. A person of skill in the art cannot immediately envision all the possible chemical structures for a "masked acid" with this function. Thus, the metes and bounds of the claimed invention cannot be determined. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169.

Finally, as stated previously simply providing an example of a masked acids (e.g., 1,4-cyclohex-2-3-enediylbis(pentafluorobenzoate)) does not allow a person of skill in the art to determine *a priori* all the possible compounds that would fall within this category. Conceivably, any compound could be a masked acid given an infinite number of chemical transformations. Therefore, the rejection is maintained for the reasons of record.

Claims Rejections - 35 U.S.C. 102

5. Claims 1-2, 6, 12, 15, 52, 53, 56, 57, 70-71 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by Holmes, C. P. (US #5,242,974) (Filing Date is **Nov. 22, 1991**; Date of Patent is **Sep. 7, 1993**).

For ***claims 1,15,52,70***, Holmes, C. P. (see entire document) teaches methods for the light generated autocatalytic removal of protecting groups in solid-phase synthesis (see Holmes, C. P., column 4, lines 59-64) (A protecting group "may be selectively removed there from for exposure of a reactive group"), which anticipates claim. For example, Holmes, C. P. teaches that the protecting group can be removed from a "synthetic intermediate" on a "surface" (see Holmes, C. P., column 2, lines 44-60) (Holmes states that protecting groups may be used in conjunction with resin bound intermediates to synthesize polymers using "intermediates" of shorter length) (see also Holmes, C. P., column 4, lines 48-50) (A substrate or support is defined as a material or group of materials having a rigid or semi-rigid "surface or surfaces"). In addition, Holmes, C. P. discloses the "photolabile" NVOC protecting group (see Holmes, C. P., column 18, lines 43-54), which can act as a "radiation sensitive compound", a "catalyst", and an "autocatalytic compound." The Examiner contends that the NVOC protecting group can function as a radiation sensitive compound because NVOC is cleaved into 6,6-bisveratric acid by light and thus it is "sensitive" to light (see Holmes, C. P., column 18, lines 43-54). Furthermore, the Examiner contends NVOC can function as a catalyst (6,6-bisveratric acid catalyzes the removal of the NVOC protecting group) and an autocatalyst (6,6-bisveratric acid catalyzes the formation of more 6,6-bisveratric acid) because the NVOC protecting group is an acid-labile protecting group (see column 19, lines 29-30 showing the susceptibility of NVOC to acid cleavage) and thus will be susceptible to further acid cleavage by the 6,6-bisveratric acid that is produced during the course of the light initiated reaction. "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Furthermore, Holmes, C. P. teaches "light-directed, spatially-addressable techniques" for removing protecting groups (see Holmes, C. P., column 2 lines 32-32) wherein the protecting group is removed by "irradiating at least a part of said surface." In addition, Holmes, C. P. discloses removing the NVOC group with hv and reacting the resulting functional group with synthetic monomer intermediates (se Holmes, C. P. i.e., the '974 patent, figure 5, outlining the reaction of NVOC with *hv* and monomers).

Finally, Holmes, C. P. teaches "light-directed, spatially-addressable techniques" for removing protecting groups (see Holmes, C. P., column 2 lines 32-32).

For ***claim 2***, Holmes, C. P. teaches a "photoremovable" NVOC protecting group (see Holmes, C. P., column 6, lines 21-22; column 18, lines 43-54), which reads on claim 2 wherein the radiation sensitive compound of claim 1 is a "photosensitive compound or group."

For ***claim 6***, Holmes, C. P. teaches synthesizing various types of polymers including "peptides" (see Holmes, C. P., column 9, lines 5) ("In a preferred embodiment for peptide synthesis, the protective group PG1 is removed with light"), which reads on claim 6 wherein "said synthesis intermediate is ... a polypeptide."

For ***claim 12***, Holmes, C. P. teaches a photolabile NVOC protecting group that is cleaved into an acid catalyst (6,6-bisveratric acid) by light (see Holmes, C. P., column 18, lines 43-54), which reads on claim 12 wherein "said photosensitive compound is ... a photoactivated acid catalyst."

For ***claim 53***, Holmes, C. P. teaches a "photoremovable" NVOC protecting group that is cleaved into an acid catalyst i.e., 6,6-bisveratric acid (see Holmes, C. P., column 6, lines 21-22; column 18, lines 43-54), which reads on claim 53 wherein "the photosensitive compound or group is a photoactivated acid catalyst."

For ***claim 56***, Holmes, C. P. teaches synthesizing various types of polymers including "peptides" (see Holmes, C. P., column 9, lines 5) ("In a preferred embodiment for peptide synthesis, the protective group PG1 is removed with light"), which reads on claim 56 wherein "said synthesis intermediate is ... a polypeptide."

For ***claim 57***, Holmes, C. P. teaches an acid labile NVOC protecting group (see Holmes, C. P., column 18, lines 43-54), which reads on claim 57 wherein "the removable protecting group is an acid removable group."

For ***claim 71***, Holmes, C. P. teaches a "photoremovable" NVOC protecting group that is cleaved into an acid catalyst i.e., 6,6-bisveratric acid (see Holmes, C. P., column 6, lines 21-22; column 18, lines 43-54), which reads on claim 71 wherein "the photosensitive compound or group is a photoactivated acid catalyst."

For ***claim 73***, Holmes, C. P. teaches synthesizing various types of polymers including "peptides" (see Holmes, C. P., column 9, lines 5) ("In a preferred embodiment for peptide synthesis, the protective group PG1 is removed with light"), which reads on claim 73 wherein "said synthesis intermediate is ... a polypeptide."

Response

6. Applicant's arguments directed to the above anticipation rejections over the Holmes et al were fully considered but not found persuasive for the reasons outlined below. Please note that the original rejections have been modified to more clearly address applicants' amendments and/or arguments.

For Holmes et al, Applicants argue that the '773 patent does not prove that NVOC (or 6,6-bisveratric acid) is "inherently" functioning as a "catalyst" or an "autocatalyst" i.e., the burden to prove inherency has not been met (see Paper No. 21, pages 10-12).

The Examiner concedes that the inherency burden has not been met using the '773 patent. However, the Examiner does not concede that the '924 patent would not anticipate Applicants' claimed invention (see newly amended rejection above). Here, the Examiner contends that the Office does not have the facilities to test whether or not the NVOC protecting group is or is not functioning as a "catalysts" and/or a "autocatalyst" and, as a result, it is Applicants' burden to prove that it is not (see newly amended rejection above).

7. Claims 1-3, 12, 52-54, 57, 60, 70-71, 76 are rejected under 35 U.S.C. 102(b) as being anticipated by MacDonald et al (MacDonald, S. A.; Willson, C. G.; Frechet, J. M. "Chemical Amplification in High-Resolution Imaging Systems" ACC. Chem. Res. **1994**, 27(6):151-158.

For ***claims 1,52,70***, MacDonald et al teaches a light activated autocatalytic method for the removal of the *t*-BOC protecting groups (see MacDonald et al, page 152, column 2, last paragraph; see also page 153, figure 3), which anticipates claim 1. For example, MacDonald et al teaches applying to a surface a "*t*-boc resist" (i.e., a "catalyst system", see MacDonald et al, page 153, figure 2 wherein a *t*-boc resist is applied to the surface; see also page 152, column 2, last paragraph). Here, triphenylsulfonium hexafluoroantimonate (i.e., a radiation sensitive compound) produces "H^+" (i.e., an acid catalyst) when it is irradiated (see MacDonald et al, page 153, figure 3, first reaction scheme showing light activation of triphenylsulfonium hexafluoroantimonate). In addition, MacDonald et al teaches that the "H^+" (i.e., the catalyst) can "activate" the *t*-BOC protecting group (i.e., the t-BOC protecting groups function as BOTH a "protecting group" AND a catalyst activated "autocatalytic compound") to generate a *t*-Butyl cation (i.e., a protecting group removing product) that can cleave more t-BOC protecting groups when it regenerates the "H^+" (see MacDonald et al, figure 3, last reaction wherein the *t*-Butyl cation that is used to cleave the carboxylic acid is "regenerated" i.e., the *t*-Butyl cation breaks down into isobutylene and H^+). Furthermore, MacDonald et al discloses

the unprotected PBOCST (i.e., a synthetic intermediate) reacting with Me2N-SiMe3 (see figure 11).

For ***claim 2***, MacDonald et al teaches triphenylsulfonium hexafluoroantimonate as a light sensitive compound that generates an acid catalyst upon exposure to light (see MacDonald et al, page 152, last paragraph), which reads on claim 2 wherein the radiation sensitive compound of claim 1 is a "photosensitive compound or group."

For ***claims 3,54***, MacDonald et al discloses t-Boc, which is a "masked acid" (see page 153, figure 3).

For ***claim 12***, MacDonald et al teaches triphenylsulfonium hexafluoroantimonate that is converted via light to trifluoromethane sulfonic acid, which reads on claim 12 wherein "said photosensitive compound is ... a photoactivated acid catalyst."

For ***claim 53***, MacDonald et al teaches triphenylsulfonium hexafluoroantimonate that is converted via light to trifluoromethane sulfonic acid (see MacDonald et al, page 152 second column), which reads on claim 53 wherein "said photosensitive compound is ... a photoactivated acid catalyst."

For ***claim 57***, MacDonald et al teaches the t-BOC protecting group that can be hydrolyzed in acid (see MacDonald et al, page 152, second column), which reads on claim 57 wherein "the removable protecting group is an acid removable group."

For ***claim 60***, MacDonald et al teaches the t-BOC protecting group (see MacDonald et al, page 152, second column), which reads on claim 60 wherein "the protecting group is selected from ... *tert*-butyloxycarbonyl."

For ***claim 71***, MacDonald et al teaches triphenylsulfonium hexafluoroantimonate that is converted via light to trifluoromethane sulfonic acid, which reads on claim 72 wherein "said photosensitive compound is ... a photoactivated acid catalyst."

For ***claim 76***, MacDonald et al teaches the *t*-BOC protecting group (see MacDonald et al, page 152, second column), which reads on claim 60 wherein "the protecting group is selected from ... *tert*-butyloxycarbonyl."

Response

8. Applicant's arguments directed to the above anticipation rejections over the MacDonald et al were fully considered but not found persuasive for the reasons outlined below. Please note that the original rejections have been modified to more clearly address applicants' amendments and/or arguments.

For Macdonald et al, applicants argue that **[a]** triphenylsulfonium hexafluoroantimonate is not an autocatalyst as defined by the pending claims and, as a result, MacDonald fails to disclose an autocatalytic compound or group as defined by independent claims 1 and 52 and

dependent claim 15 because Macdonald et al does not teach the acid catalyzed decomposition of the triphenylsulfonium hexafluoroantimonate i.e., it only teaches the light catalyzed degradation and thus does not catalyze the ***same*** reaction (see Paper No. 21, page 14), **[b]** MacDonald fails to disclose a synthesis intermediate and, as a result does not anticipate claim 70. Applicants further state that the Examiner has not demonstrated "how PBOCST (with the t-BOC protecting group removed) is capable of reacting with more PBOCST" and, as a result, "misses the mark as MacDonald's teaching of unprotected PBOCST reactin with Me2N-SiMe3 is only a teaching of unprotected PBOCST reacting with another compound, which is only have of the definition of Applicants' "synthess intermediate", **[c]** MacDonald does not disclose the synthetic intermediates in claim 6.

The Examiner **[a]** concedes that MacDonald et al does not teach an acid catalyzed degradation of triphenylsulfonium hexafluoroantimonate (the reference simply does not address this point) and, as a result, the Examiner concedes that triphenylsulfonium hexafluoroantimonate cannot function as an "autocatalyst" as defined by Applicants' specification. However, the Examiner does NOT concede that MacDonald fails to teach an "autocatalytic" compound as defined by independent claims 1 and 52 and dependent claim 15 (see newly modified rejection above). Here, the Examiner contends that the *t*-BOC protecting group can function as BOTH a "protecting group" and an "autocatalyst" within the scope of Applicants claims because it can produce a "protecting group removing product" (i.e., the *t*-butyl cation ↔ isobutylene/H+), which further removes t-BOC protecting groups (i.e., is autocatalytic) upon "activation" (i.e., cleavage from the polymer) by the light generated catalyst (i.e., the sulfonic acid).

The Examiner further contends that **[b]** in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that PBOCST must react with another PBOCST to anticipate Applicants' claims) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Here, the definition of "synthetic intermediate" could reasonably be interpreted to include a compound that participates in an organic reaction. Therefore, the unprotected PBOCST qualifies as a synthetic intermediate because it is an "intermediate" product i.e., PBOCST → unprotected-PBOCST → PBOCST-$SiMe_3$, wherein the "unprotected-PBOCST" is clearly an synthetic "intermediate" in this set of reactions.

The Examiner **[c]** concedes to Applicants' arguments with regard to claim 6 and this claim has been removed from the newly amended rejection (see above).

New Rejections

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such

a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

These claims encompass a broad genus. For example, claim 1 outlines method steps for the removal of a "protecting group" from a "linker molecule" or a "synthesis intermediate" by applying to a surface a "catalysts system" that comprises a "radiation sensitive compound" that will product a "catalysts" and an "autocatalytic compound" that will produce a "protecting group removing product" when activated by said catalyst. The scope of this claim includes an infinite number of methods using an infinite number of protecting groups, linker molecules, synthesis intermediates, radiation sensitive compounds, catalysts, autocatalysts and protecting group removing products wherein no distinguishing structural attributes are provided for any of these compound and/or chemical functionalities. The specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the protecting groups, linker molecules, synthesis intermediates, radiation sensitive compounds, catalysts, autocatalysts and protecting group removing products. Although the specification discloses a few examples e.g., toluenesulfonic acid as a PAAC, 1,4-cyclohex-2-enediylbis-(pentafluorobenzoate) and an enhancer in polynucleotide synthesis in Examples 1-2; the PAC and enhancer shown in figure 3 again used in polynucleotide synthesis (see specification, Examples), the specification and claims do not provide ***any*** guidance as to what structural features ***all*** of these protecting groups, linker molecules, synthesis intermediates,

radiation sensitive compounds, catalysts, autocatalysts and protecting group removing products. Consequently, it is not possible to determine *a priori* which compounds would be encompassed by these broad claims because there is no common structural attributes that can link together ***all*** of these potential protecting groups, linker molecules, synthesis intermediates, radiation sensitive compounds, catalysts, autocatalysts and protecting group removing products i.e., there is no teaching that would allow a person of skill in the art to determine *a priori* ***all*** the different types of compounds that should be included in this genus from the few examples provide by applicants.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify ***all*** of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant, listing a few examples like toluenesulfonic acid and pentafluorobenzoate (see specification, Examples) is insufficient to teach the entire genus. Furthermore, it is well recognized in the art that this area of research is highly unpredictable and thus the level of skill in the art cannot compensate for the deficiencies in the disclosure because not all "catalyst systems" are compatible with solid-phase synthesis (e.g., "catalysts systems" employing alkaline conditions would hydrolyze the oligonucotide protecting groups essential for solid-phase synthesis, see McGall, G. Labadie, J.; Brock, P.; Wallraff, G.; Nguyen, T.; Hisberg, W. "Light-directed synthesis of high-density oligonucleotide arrays using semiconductor photoresists" *PNAS* **1996**, *93*, 13555-135600, especially page 13556, column 2, last two paragraphs). Consequently, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative

number of species to describe this enormous genus. Thus, applicant was not in possession of the claimed genus.

10. Claims 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotide synthesis using toluenesulfonic acid as a PAAC, 1,4-cyclohex-2-enediylbis-(pentafluorobenzoate) and an enhancer and the compounds shown in Example 3 (see specification, pages 30-31), does not reasonably provide enablement for any protecting groups, linker molecules, synthesis intermediates, radiation sensitive compounds, catalysts, autocatalysts and protecting group removing products. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". Some of these factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims are drawn to a broad genus. The scope of this claim includes an infinite number of methods using an infinite number of protecting groups, linker molecules, synthesis intermediates, radiation sensitive compounds, catalysts, autocatalysts and protecting group removing products wherein no distinguishing structural attributes are provided for any of these compound and/or chemical functionalities. The specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the protecting groups, linker molecules, synthesis intermediates, radiation sensitive compounds, catalysts, autocatalysts and protecting group removing products. Consequently, the nature of the invention cannot be fully determined because the invention has not been defined with particularity.

(3 and 5) The state of the prior art and the level of predictability in the art: The art is unpredictable. For example, it has been found that photolytic removal of protecting groups leads to "synthetic intermediates" of poor chemical quality and results in diminished yields after repetitive coupling steps (see Pirrung, M. C.; Bradley, J. C. "Comparison of Method for Photochemical Phosphoramidite-Based DNA Synthesis" *J. Org. Chem.* **1995**, *60*, 6270-6276). The diminished yields do not appear to be due to irradiation per se, but are intrinsic to the process of photochemical deprotection. A later publication further disclosed that the process never adequately produced useful peptide arrays (see David Stipp, "Gene Chip Breakthrough," Fortune pp. 56-73, March 31, 1997). Thus a parallel placement method for use in the preparation of arrays of organic compounds is not presently available. Therefore, the Examiner contends that the level of predictability in the art is low or absent.

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants provide only examples of "acid" photoactivated catalysts used solely for polynucleotide synthesis.

(8) The quantity of experimentation needed to make or use the invention base on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have not provided any working examples that would teach this enormous genus that falls within a highly unpredictable art area. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are rejected because the "radiation sensitive" compound in these claims is not defined with any chemical or physical characteristic, but only by functional properties i.e., its sensitivity to radiation. A claim to a material defined solely in terms of what it can do, or a property thereof, does not particularly point out the claimed invention. A person of skill in the art cannot immediately envision all the possible chemical structures for a peptide with this function. Thus, the metes and bounds of the claimed invention cannot be determined. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169.

B. Claims 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are rejected because the "autocatalytic" compound in these claims is not defined with any chemical or physical characteristic, but only by functional properties i.e., its ability to function as an autocatalyst. A claim to a material defined solely in terms of what it can do, or a property thereof, does not particularly point out the claimed invention. A person of skill in the art cannot immediately envision all the possible chemical structures for a peptide with this function. Thus, the metes and bounds of the claimed invention cannot be determined. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169.

C. Claims 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are rejected because the "protecting group removing" product in these claims is not defined with any chemical or

physical characteristic, but only by functional properties i.e., its ability to remove protecting groups. A claim to a material defined solely in terms of what it can do, or a property thereof, does not particularly point out the claimed invention. A person of skill in the art cannot immediately envision all the possible chemical structures for a peptide with this function. Thus, the metes and bounds of the claimed invention cannot be determined. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169.

D. Claims 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are rejected because the compounds that comprise the "catalyst system" are not defined with any chemical or physical characteristic, but only by functional properties i.e., their ability to function as catalysts or enhancers. A claim to a material defined solely in terms of what it can do, or a property thereof, does not particularly point out the claimed invention. A person of skill in the art cannot immediately envision all the possible chemical structures for a peptide with this function. Thus, the metes and bounds of the claimed invention cannot be determined. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-2, 6, 12, 15, 52-54, 56-60, 70-71 and 73-76 are rejected under 35 U.S.C. 102(b) as being anticipated by Pirrung et al (U.S. Patent No. 5,143,854) (Date of Patent is **1992**).

For ***claims 1-2, 6, 12, 15, 52-54, 56-60, 70-71, 73-76***, Pirrung et al (see entire document) discloses synthesis of polypeptide arrays using a photoremovable protecting group including NVOC (which also acts as an autocatalytic compound, see above 35 U.S.C. § 102 rejection for Holmes), which anticipates claim 1 (see Pirrung et al, abstract; see also column 3; see also figures 1-7 & 14A). As shown in the reference polypeptides are built up on a substrate using amino acids with photoremovable protecting groups such as NVOC which reads on the claimed "synthesis intermediates" and "photosensitive protecting groups". The protecting groups are selectively removed by irradiation through a mask; this is performed to create a desired sequence (e.g., see column 28, lines 12-66, which teaches the monomer-by-monomer synthesis of the sequence YGGFL; see also column 6, lines 9-21, especially line 14, wherein Pirrung et al also teaches that nucleotides can be used as monomers in their method. The reference also teaches that contrast enhancement materials can be applied between the mask and the substrate to "enhance contrast of light applied to the substrate" (see column 14, lines 5-16). Molecules such as "quinone diazid" compounds are taught (see column 14, line 10).

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-79 of copending Application No. 09/922,426 (Pub. No.: US 2002/0022721 A1) (referred to herein as '721), especially claims 1-16. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims are either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986). For example claim 1 of the present application is generic to all that is recited in claims 1 of '721. That is, claim 1 of '721 falls entirely within the scope of claim 1 of the present application or, in other words, claim 1 of the present application is anticipated by claims 1 of '721. Specifically, **[1]** "a method for removing a protective group from a synthesis intermediate" in claim 1 of '721 falls entirely within the scope of "a method for removing a protecting group from a linker molecule

OR a synthesis intermediate" in claim 1 of the present application, **[2]** "a photosensitive compound or group" in claim 1 of '721 falls entirely within the scope of a "radiation sensitive compound or group" in claim 1 of the present application, **[3]** said photosensitive compound or group producing a catalyst when irradiated" in claim 1 of '721 falls entirely within the scope of "said radiation sensitive compound or group producing a catalyst when irradiated in claim 1 of the present application, **[4]** both claim 1 of '721 and claim 1 of the present application disclose the same autocatalytic compound or group, **[5]** both claim 1 of '721 and claim 1 of the present application disclose irradiating at least a part of said surface to remove said protecting group. Claim 1 of '721 further discloses the use of a compound capable of introducing latency. This limitation would also fall within the scope of claim 1 of the present application because it employs "comprising" terminology.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claim 1-3, 6, 12, 14-15, 52-54, 56-60, 70-71 and 73-76 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 (especially claim 18) of U.S. Patent 6,083,697 (referred to as '697).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226

(Fed. Cir. 1998); *In re Goodman,* 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986).

Although the conflicting claims are not identical, they are not patentably distinct from each other (see all claims of '697 to present application, especially those claims outlined below). Both inventions are directed to methods steps for removing a protecting group on a substrate surface using a catalyst system.

The present claims differ from the method of claim 18 in '697 in that claim 18 does not recite the use of a "radiation sensitive" compound. However, Applicants specification defines a "catalyst system" (a term that is used in claim 18) as a "photo activated catalyst" and claims 1-17 also disclose radiation sensitive compound e.g., see claim 1.

It would have been obvious to combine the claims of '697 to render obvious the claims of the present application because the claims of '697 teach a generic method (i.e., claim 18 is drawn to a method for removing protecting groups using a catalyst system) and then further teaches more specific embodiments (i.e., claims 1-17 are drawn to an apparatus that is to be used in conjunction with the method), wherein the other claims (and specification definitions) teach toward applicants' claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (703) 308-2423. The examiner can normally be reached Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-2439.

Jon D. Epperson, Ph.D.
August 17, 2003

BENNETT CELSA
PRIMARY EXAMINER